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Accuracy of Dobutamine Echocardiography for Detection of Myocardial Viability in Patients With an Occluded Left Anterior Descending Coronary Artery

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Objectives. **We studied the accuracy of dobutamine echocardiography for the detection of myocardial viability in patients with an occluded left anterior descending coronary artery and regional ventricular dysfunction.**

Background. **Contractile reserve during dobutamine echocardiography is an accurate marker of myocardial viability in patients with coronary stenoses and ventricular dysfunction. However, its accuracy in patients with an occluded vessel has not been evaluated.**

Methods. **We studied 41 patients with >50% stenosis of the left anterior descending coronary artery and regional ventricular dysfunction who underwent dobutamine echocardiography for detection of viable myocardium. Contractile reserve was defined as improvement in wall motion score of two or more contiguous septal or anterior segments during dobutamine echocardiography. Recovery of function was defined as improvement in rest wall motion score of two or more contiguous segments after revascularization.**

Results. **Patients were classified into two groups according to the presence (n = 20) or absence (n = 21) of left anterior descending coronary artery occlusion. Contractile reserve was detected in 40% of patients with an occluded and 43% with a nonoccluded artery (p = 0.8). Of 41 patients, 27 underwent revascularization, 12 with and 15 without an occluded vessel. Recovery of function occurred in 6 (50%) of 12 patients in the occluded artery group and in 5 (33%) of 15 in the nonoccluded artery group (p = 0.4). Among patients with an occluded artery, the positive and negative predictive values of dobutamine echocardiography for recovery of function were 100% (95% confidence interval [CI] 48% to 100%) and 86% (95% CI 42% to 100%), respectively.**

Conclusions. **Our results indicate that contractile reserve during dobutamine echocardiography can be detected in patients with an occluded vessel and may be useful for predicting recovery of function after revascularization.**

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In patients with coronary artery disease and regional left ventricular dysfunction, the presence of contractile reserve during dobutamine echocardiography identifies viable myocardium and predicts recovery of ventricular function after revascularization (1–8). In patients with recent myocardial infarction, revascularization can result in recovery of ventricular function, even in territories that are perfused only by collateral flow (9). However, it is not known whether collateral-dependent, dysfunctional but viable myocardium retains inotropic contractile reserve. Therefore, we sought to assess the accuracy of contractile reserve during low dose dobutamine echocardiography for the detection of myocardial viability in patients with an occluded left anterior descending coronary artery and regional ventricular dysfunction.

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Methods

Patients. Subjects for this study were selected from a consecutive group of patients who underwent low dose dobutamine echocardiography for the assessment of myocardial viability as part of an ongoing prospective protocol at our institution (1,6). According to this protocol, all patients undergoing coronary angiography are screened, and those with stable coronary artery disease and rest regional left ventricular dysfunction undergo dobutamine echocardiography to assess myocardial viability. Patients with a recent (<1 week) myocardial infarction, unstable angina, >50% left main stenosis, significant valvular disease, a previous coronary artery bypass graft surgery or technically inadequate echocardiographic images are excluded. From this data base, patients meeting the following criteria were included in the study: 1) presence of >50% diameter stenosis in the left anterior descending coronary artery; and 2) rest regional wall motion abnormalities in at least two adjacent segments in the left anterior descending coronary artery territory, seen on two-dimensional echocardiography.

Echocardiographic protocol. After providing written informed consent, all patients underwent dobutamine echocardiography according to the following protocol. First, a rest

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two-dimensional echocardiogram was recorded in the left lateral decubitis position, using a Vingmed CFM 750 equipped with a 3.25-MHz transducer (Vingmed Sound, Horten, Norway). Standard parasternal and apical views were obtained and recorded on 0.5-in. VHS tape. Next, a dobutamine infusion was started at 5 μg/kg body weight per min and increased every 3 min to 10, 15 and 20 μg/kg per min. Echocardiographic images were recorded at the end of each dose. During dobutamine infusion, blood pressure and cardiac rhythm were monitored. The infusion was terminated prematurely if any of the following occurred: severe angina, systolic blood pressure <80 or >220 mm Hg, >85% of predicted maximal heart rate, new or worsening wall motion abnormalities in at least two adjacent segments or significant arrhythmias. In patients who subsequently underwent revascularization, a rest two-dimensional echocardiogram was obtained 4 weeks after the procedure. The decision for revascularization was made before, and not based on, the dobutamine echocardiographic results.

Echocardiographic analysis. The rest and dobutamine-echocardiographic images were digitized into a Macintosh IIci computer using EchoPac 4.2 (Vingmed Sound) to allow display of one cardiac cycle in a continuous loop format. A quad screen format was used to allow simultaneous comparison of rest and dobutamine images. All echocardiograms were interpreted by an experienced investigator blinded to the clinical and coronary angiographic data. For analysis, the left ventricle was divided into 16 segments, as recommended by the American Society of Echocardiography (10). Wall motion was assessed visually using both endocardial motion and wall thickening. A wall motion score was given to each segment as follows: 1 = normal; 2 = hypokinetic; 3 = akinetic; and 4 = dyskinetic. Wall motion of all visualized segments was scored at rest and at each dobutamine dose. The left anterior descending coronary artery territory was defined as base, mid and distal segments of the anterior septum and anterior wall. Contractile reserve in the left anterior descending coronary artery territory was defined as ≥1 grade improvement in wall motion score in at least two adjacent segments during dobutamine infusion. For dyskinetic segments, the improvement in wall motion score had to be >1 grade.

In patients who had follow-up echocardiograms after revascularization, rest wall motion was similarly scored by an experienced investigator (P.A.G.) who had no knowledge of the clinical data and preoperative dobutamine-echocardiographic results. Recovery of function in the left anterior descending coronary artery territory was defined as ≥1 grade improvement in wall motion score of at least two adjacent septal or anterior segments compared with the preoperative rest study. For segments with dyskinesia on the preoperative echocardiogram, recovery was defined as >1 grade improvement in wall motion score. For both preoperative and postoperative rest echocardiograms, a wall motion score index was derived (the sum of individual wall motion scores divided by the respective number of segments) for the entire ventricle as well as the left anterior descending coronary artery territory (2).

Coronary angiographic analysis. Coronary angiography was performed within 24 h of the dobutamine-echocardiogram. All coronary angiograms were analyzed by an investigator who had no knowledge of the results of the echocardiograms. Each vessel was visualized in multiple views, and the most severe-appearing lesion was selected for analysis. Percent diameter stenosis was determined quantitatively using Cardiovascular Angiography Analysis System (Rotterdam, The Netherlands) (11). Vessel occlusion was defined as a lesion with no anterograde distal flow. The site of stenosis or occlusion was noted. Lesions proximal to the first major septal or diagonal segment were classified as "proximal" and lesions between the first major septal and diagonal segment were classified as "mid." The presence or absence of significant angiographic collateral channels to the left anterior descending coronary artery was also noted. Significant collateral channels were defined as the presence of angiographically visible retrograde flow filling at least part of the epicardial segment of the occluded artery.

Statistical analysis. All values are reported as mean value ± SD. Patients with occluded versus nonoccluded arteries were compared using chi-square analysis for categorical variables and the unpaired *t* test for continuous variables. Chi-square analysis was used to assess whether the presence of contractile reserve predicted recovery of rest function after revascularization in patients with and without left anterior descending coronary artery occlusion.

Results

Patient characteristics. Among patients who underwent coronary angiography at our institution between July 1990 and January 1995, 85 consecutive patients met the criteria of our protocol and underwent dobutamine echocardiography. Of these, 21 patients did not have left anterior descending coronary artery stenosis, and an additional 18 had normal rest wall motion in the left anterior descending coronary artery territory. Five patients were excluded because their angiograms could not be located for analysis. The remaining 41 patients, with >50% stenosis of the left anterior descending coronary artery along with rest wall motion abnormalities in two or more segments in that territory, formed the study group. These patients underwent coronary angiography for either angina (61%), congestive heart failure (22%) or an ischemic response on a stress test (17%). All patients were men (mean age 59 ± 8 years). These patients were divided into two groups: 20 patients with occlusion of the left anterior descending coronary artery (Group I) and 21 patients with a stenosed but patent left anterior descending coronary artery (Group II). Table 1 compares the clinical, angiographic and baseline echocardiographic characteristics of the two groups. The groups were similar with respect to age, history of infarction, prevalence of angina, multivessel disease, baseline ejection fraction and preoperative rest wall motion score index. The location of the lesion was proximal in 7 (35%) of Group I and 10 (47%) of Group II patients ($p = 0.4$). In Group II, mean stenosis in the left anterior descending coronary artery was 75 ± 17%.

Table 1. Comparison of Baseline Characteristics of Patients With and Without Occlusion of the Left Anterior Descending Coronary Artery

	Group I (occluded LAD) (n = 20)	Group II (patent LAD) (n = 21)	p Value
Age (yr)	60 ± 8	59 ± 9	0.6
Prior MI	15 (75)	14 (67)	0.1
Angina	15 (75)	14 (67)	0.6
CHF	4 (20)	9 (42)	0.07
Multivessel disease	19 (95)	17 (81)	0.2
% LAD stenosis	100	75 ± 17	< 0.0001
Collateral channels to LAD	15 (75)	1 (5)	< 0.0001
Rest EF (%)	31 ± 7	33 ± 8	0.6
Rest WMSI	2.2 ± 0.5	2.1 ± 0.4	0.5
Rest RWMSI	2.5 ± 0.6	2.4 ± 0.4	0.5

Data are expressed as mean value ± SD or number (%) of patients. CHF = congestive heart failure; EF = ejection fraction; LAD = left anterior descending coronary artery; MI = myocardial infarction; RWMSI = regional wall motion score index in left anterior descending artery territory; WMSI = wall motion score index.

Angiographic collateral flow to the left anterior descending coronary artery was present in 15 (75%) Group I patients compared with only 1 (5%) patient in Group II ($p < 0.0001$).

Results of dobutamine echocardiography. At baseline, 180 (73%) of 246 ventricular segments in left anterior descending coronary artery territory had abnormal wall motion. There was no difference in the rest regional wall motion score index between the two groups (Table 1). During dobutamine echocardiography, contractile reserve in the left anterior descending coronary artery territory was seen in 17 (41%) of 41 patients. Contractile reserve was present in 8 (40%) Group I and 9 (43%) Group II patients ($p = 0.8$). In patients with an occluded artery, the occurrence of contractile reserve was not predicted by the site of occlusion or the presence of angiographic collateral channels. Contractile reserve was seen in 2 (29%) of 7 patients with proximal and 6 (46%) of 13 with mid occlusion ($p = 0.4$). Among patients with left anterior descending coronary artery occlusion, contractile reserve was present in 7 (47%) of 15 with and 1 (20%) of 5 without angiographic collateral channels ($p = 0.3$). In Group II, contractile reserve was present in 5 (50%) patients with proximal and 4 (36%) with mid lesions ($p = 0.5$).

Recovery of regional function after revascularization. The decision to perform revascularization was made before the interpretation of dobutamine-echocardiography. Of 41 patients, 27 (66%) were revascularized by either coronary artery bypass graft surgery (n = 24) or percutaneous transluminal coronary angioplasty (n = 3). Revascularization was performed in 12 (60%) of 20 patients with occluded and 15 (71%) of 21 with nonoccluded left anterior descending arteries ($p = 0.6$). None of the patients had any cardiac events between the baseline and follow-up echocardiographic studies.

On follow-up, 11 (41%) patients showed recovery of regional wall motion in the left anterior descending coronary artery territory, with a decrease in the regional wall motion score index from 2.3 ± 0.4 to 1.8 ± 0.5 ($p = 0.002$). Recovery of function occurred in 6 (50%) of 12 patients with an occluded and 5 (33%) of 15 with a nonoccluded artery ($p = 0.6$). Recovery of function was not affected by the site of the lesion and occurred in 6 (55%) patients with proximal and 7 (44%) with mid lesions ($p = 0.6$).

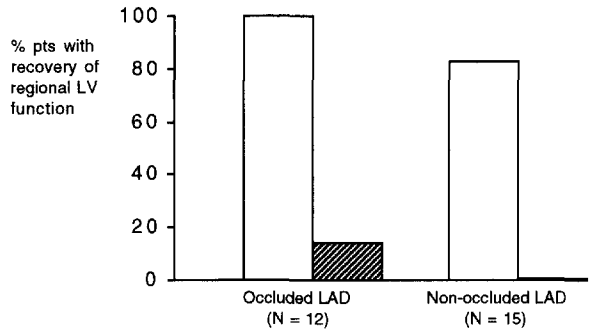

Figure 1. Comparison of the predictive accuracy of contractile reserve (CR) during dobutamine echocardiography for the recovery of regional left ventricular (LV) function in patients (pts) with and without left anterior descending coronary artery (LAD) occlusion who underwent revascularization. **Open columns** = patients with contractile reserve; **hatched column** = patients without contractile reserve.

Accuracy of contractile reserve for predicting recovery of ventricular function. The accuracy of contractile reserve for predicting recovery of regional ventricular function after revascularization is compared in patients with and without left anterior descending coronary artery occlusion (Fig. 1). Contractile reserve was present in five patients and absent in seven patients who underwent revascularization for an occluded artery. All patients with contractile reserve during dobutamine-echocardiography had recovery of regional ventricular function after revascularization (positive predictive value 100%; 95% confidence interval [CI] 48% to 100%). Recovery of function occurred in only one of seven patients without contractile reserve (negative predictive value 86%; 95% CI 42% to 100%). The positive and negative predictive values of contractile reserve for recovery of function in patients without left anterior descending coronary artery occlusion were 83% (95% CI 36% to 99%) and 100% (95% CI 58% to 100%), respectively. Overall, the accuracy of contractile reserve for the prediction of recovery of function was similar for patients with and without left anterior descending coronary artery occlusion (92% vs. 93%, $p = 0.8$).

Discussion

The accuracy of dobutamine echocardiography for the detection of myocardial viability in patients with coronary artery disease and ventricular dysfunction is well established (1–8). The present study extends the application of this test to the assessment of viability in patients with occluded vessels. We compared the results of dobutamine echocardiography and the outcome of revascularization in patients with regional

ventricular dysfunction and either an occluded or a stenosed but patent left anterior descending coronary artery. In our study group, contractile reserve during dobutamine echocardiography was detected in 40% of patients with an occluded vessel and regional ventricular dysfunction. Both the prevalence and the accuracy of contractile reserve for predicting recovery of regional ventricular function after revascularization were similar in patients with and without left anterior descending coronary artery occlusion.

Myocardial viability in the region of an occluded vessel. In patients with recent myocardial infarction and an occluded infarct-related artery, recovery of ventricular function after revascularization has been previously demonstrated (9,12,13). However, few data exist regarding the effect of revascularization on ventricular function in patients with chronic coronary occlusion (14). We studied patients with chronic stable coronary artery disease and found that 50% of patients with an occluded left anterior descending coronary artery had improved regional ventricular function after revascularization.

Preservation of myocardial viability in the distribution of an occluded vessel is dependent on collateral circulation (9,12,14–18). In our study, significant angiographic collateral channels were seen in 75% of patients with an occluded left anterior descending coronary artery. However, angiographic collateral channels did not predict recovery of ventricular function in our study group. Recovery of function after revascularization was seen in 57% of patients with and 40% without angiographic collateral channels ($p = 0.5$). This is in agreement with the findings of Sabia et al. (9), who demonstrated that in patients with a recent myocardial infarction and occluded vessels, collateral perfusion can be demonstrated by contrast echocardiography, even in the absence of angiographic collateral channels. The presence of collateral perfusion, as demonstrated by contrast echocardiography, identifies viable myocardium and predicts recovery of ventricular function after revascularization (6,9,12,19,20). However, this test requires cardiac catheterization and intracoronary administration of contrast agents (21). Our results indicate that low dose dobutamine echocardiography is an accurate noninvasive test for the assessment of myocardial viability in patients with occluded vessels and regional ventricular dysfunction.

Contractile reserve in collateral-dependent myocardium. This is the first study to show that collateral-dependent myocardium is capable of responding to an inotropic stimulus. The mechanism of this response was not investigated in our study. Animal experiments have demonstrated preservation of inotropic response to dobutamine, despite severe stenosis and rest hypoperfusion (22,23). The presence of contractile reserve instead of ischemia during dobutamine stimulation indicates that microvascular flow reserve was present in our patients. It has also been recently shown that collateral channels have a vasodilator reserve and blood flow can be increased by pacing, dipyridamole and nitrates (14,24,25). It is conceivable that low dose dobutamine echocardiography stimulates collateral blood flow, which in turn improves contractile performance.

Study design. We chose to study patients with left anterior descending coronary artery occlusion for several reasons. In anterior and anteroseptal myocardial segments, the left anterior descending coronary artery is the only source of anterograde blood flow with little overlap from other vessels. For an occluded left anterior descending coronary artery, the collateral-dependent myocardial segments can therefore be reliably defined. Compared with other vessels, the left anterior descending coronary artery has a greater impact on ventricular function and prognosis (26,27). In addition, the status of the left anterior descending coronary artery and its myocardial bed is often the most important consideration in planning revascularization procedures (28). We terminated the dobutamine infusion at 20 μg/kg per min because only low doses are required to elicit contractile reserve, with ischemia occurring at higher doses (2). To avoid potential error in scoring wall motion due to translation or tethering, visual assessment of wall thickening, in addition to endocardial excursion, was also used (29). We also required an improvement in wall motion score of at least two contiguous segments to define recovery of regional ventricular function. All echocardiograms were interpreted without knowledge of clinical or angiographic data.

Study limitations. The major limitation of our study is the small number of patients. We did not perform repeat angiography to confirm patency of left anterior descending coronary artery at the time of follow-up echocardiography. However, no clinical cardiac events occurred during the time between revascularization and follow-up echocardiograms. Although analysis for this study was done retrospectively, patients were selected from a cohort prospectively enrolled in a protocol evaluating the accuracy of dobutamine-echocardiography for the detection of myocardial viability. Patients with and without left anterior descending coronary artery occlusion were well matched for baseline clinical and echocardiographic characteristics. Because the decisions regarding angiography and revascularization were based on clinical considerations, the prevalence of contractile reserve and reversible dysfunction in our study patients may be higher than that in the general population. However, there was no difference in the occurrence of these findings between patients with an occluded versus a nonoccluded vessel. The overall prevalence of myocardial viability in our study was also similar to that reported in previous studies of patients with coronary artery disease and ventricular dysfunction (1–6). Not all the patients in our study were revascularized, which may potentially bias the assessment of the predictive accuracy of contractile reserve. Because the results of dobutamine echocardiography were available to the patients' physicians, the decision to revascularize could have been potentially biased by the outcome of the test. However, the decision to revascularize was made before the interpretation of dobutamine echocardiography. This is reflected by the similar prevalence of contractile reserve among revascularized and nonrevascularized patients (41% vs. 43%, $p = 0.9$).

Conclusions. Our data suggest that contractile reserve during low dose dobutamine echocardiography is useful for the detection of viable myocardium in patients with an occluded

left anterior descending coronary artery, and may predict recovery of regional ventricular function after revascularization. These findings should be confirmed in a larger prospective study.

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